

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Jeppesen et al.

Application No.: To be assigned

Group Art Unit: To be assigned

Filed: November 27, 2001

Examiner: To be assigned

For: New Compounds, Their Preparation and Use

PRELIMINARY AMENDMENT

Commissioner for Patents
Washington, DC 20231

Sir:

Before the above-captioned application is taken up for examination, entry of the following amendment is respectfully requested:

IN THE SPECIFICATION:

At page 1, after the title, insert

--CROSS-REFERENCE TO RELATED APPLICATIONS

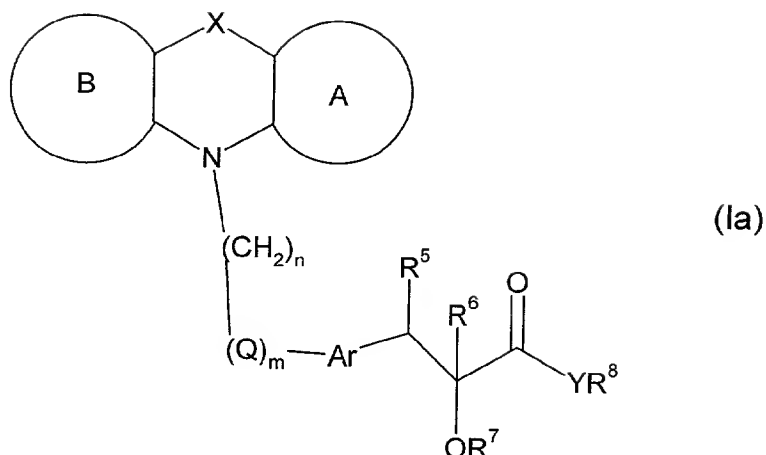
This application is a divisional of U.S. Serial No. 09/420,347 filed on October 19, 1999, and claims priority under 35 U.S.C. 119 of Danish application PA 1998 01354 filed on October 21, 1998 and of U.S. provisional application no. 60/105,913 filed on October 28, 1998, the contents of which are fully incorporated herein by reference.--

IN THE CLAIMS:

Please cancel claims 3-6, 8-15, 17, 19-22, 25, 35, 37-42, and 45-49, without prejudice or disclaimer.

Substitute the following amended claims for the pending claims having the same claim numbers (a marked-up version pursuant to 37 C.F.R. 1.21 is attached hereto):

1. (Amended) A compound of formula (Ia)



wherein ring A, fused to the ring containing X and N, represents a 5-6 membered cyclic ring optionally substituted with one or more halogen, perhalomethyl, hydroxy, nitro, cyano, formyl, or C₁₋₁₂alkyl, C₄₋₁₂-alkenynyl, C₂₋₁₂-alkenyl, C₂₋₁₂-alkynyl, C₁₋₁₂alkoxy, aryl, aryloxy, aralkyl, aralkoxy, heterocyclyl, heteroaryl, heteroaralkyl, heteroaryloxy, heteroaralkoxy, acyl, acyloxy, hydroxyC₁₋₁₂alkyl, amino, acylamino, C₁₋₁₂alkyl-amino, arylamino, aralkylamino, aminoC₁₋₁₂alkyl, C₁₋₁₂alkoxycarbonyl, aryloxycarbonyl, aralkoxycarbonyl, C₁₋₁₂alkoxyC₁₋₁₂alkyl, aryloxyC₁₋₁₂alkyl, aralkoxyC₁₋₁₂alkyl, C₁₋₁₂alkylthio, thioC₁₋₁₂alkyl, C₁₋₁₂alkoxycarbonylamino, aryloxycarbonylamino, aralkoxycarbonylamino, -COR¹¹, or -SO₂R¹², wherein R¹¹ and R¹² independently of each other are selected from hydroxy, halogen, perhalomethyl, C₁₋₆alkoxy or amino optionally substituted with one or more C₁₋₆alkyl, perhalomethyl or aryl; optionally substituted with one or more halogen, perhalomethyl, hydroxy, nitro or cyano;

ring B, fused to the ring containing X and N, represents a 5-6 membered cyclic ring optionally substituted with one or more halogen, perhalomethyl, hydroxy, nitro, cyano, formyl, or C₁₋₁₂alkyl, C₄₋₁₂-alkenynyl, C₂₋₁₂-alkenyl, C₂₋₁₂-alkynyl, C₁₋₁₂alkoxy, aryl, aryloxy, aralkyl, aralkoxy, heterocyclyl, heteroaryl, heteroaralkyl, heteroaryloxy, heteroaralkoxy, acyl, acyloxy, hydroxyC₁₋₁₂alkyl, amino, acylamino, C₁₋₁₂alkyl-amino, arylamino, aralkylamino, aminoC₁₋₁₂alkyl,

C₁₋₁₂alkoxycarbonyl, aryloxycarbonyl, aralkoxycarbonyl, C₁₋₁₂alkoxyC₁₋₁₂alkyl, aryloxyC₁₋₁₂alkyl, aralkoxyC₁₋₁₂alkyl, C₁₋₁₂alkylthio, thioC₁₋₁₂alkyl, C₁₋₁₂alkoxycarbonylamino, aryloxycarbonylamino, aralkoxycarbonylamino, -COR¹¹, or -SO₂R¹², wherein R¹¹ and R¹² independently of each other are selected from hydroxy, halogen, perhalomethyl, C₁₋₆alkoxy or amino optionally substituted with one or more C₁₋₆alkyl, perhalomethyl or aryl; optionally substituted with one or more halogen, perhalomethyl, hydroxy, nitro or cyano;

X is -(CHR⁹)-CH₂-, -CH=CH-, -(CHR⁹)-CH=CH-, -(CHR⁹)-CH₂-CH₂-, -CH=(CR⁹)-, -(CO)-(CHR⁹)-, wherein R⁹ is hydrogen, halogen, hydroxy, nitro, cyano, formyl, C₁₋₁₂alkyl, C₁₋₁₂alkoxy, aryl, aryloxy, aralkyl, aralkoxy, heterocyclyl, heteroaryl, heteroaralkyl, heteroaryloxy, heteroaralkoxy, acyl, acyloxy, hydroxyalkyl, amino, acylamino, C₁₋₁₂alkyl-amino, arylamino, aralkylamino, aminoC₁₋₁₂alkyl, C₁₋₁₂alkoxycarbonyl, aryloxycarbonyl, aralkoxycarbonyl, C₁₋₁₂alkoxyC₁₋₁₂alkyl, aryloxyC₁₋₁₂alkyl, aralkoxyC₁₋₁₂alkyl, C₁₋₁₂alkylthio, thioC₁₋₁₂alkyl, C₁₋₁₂alkoxycarbonylamino, aryloxycarbonylamino, aralkoxycarbonylamino, -COR¹¹, or -SO₂R¹², wherein R¹¹ and R¹² independently of each other are selected from hydroxy, halogen, C₁₋₆alkoxy, amino optionally substituted with one or more C₁₋₆alkyl, perhalomethyl or aryl;

Q is -O-, -S-, >SO₂, >NR¹³, wherein R¹³ is hydrogen or C₁₋₆alkyl,

Ar represents arylene, heteroarylene, or a divalent heterocyclic group optionally substituted with one or more C₁₋₆alkyl or aryl;

R⁵ represents hydrogen, hydroxy, halogen, C₁₋₁₂alkoxy, C₁₋₁₂alkyl, C₄₋₁₂-alkenynyl, C₂₋₁₂-alkenyl, C₂₋₁₂-alkynyl or aralkyl; optionally substituted with one or more halogen, perhalomethyl, hydroxy, nitro or cyano; or R⁵ forms a bond together with R⁶,

R⁶ represents hydrogen, hydroxy, halogen, C₁₋₁₂alkoxy, C₁₋₁₂alkyl, C₄₋₁₂-alkenynyl, C₂₋₁₂-alkenyl, C₂₋₁₂-alkynyl, acyl or aralkyl; optionally substituted with one or more halogen, perhalomethyl, hydroxy, nitro or cyano; or R⁶ forms a bond together with R⁵,

R⁷ represents hydrogen, C₁₋₁₂alkyl, C₄₋₁₂-alkenynyl, C₂₋₁₂-alkenyl, C₂₋₁₂-alkynyl, aryl, aralkyl, C₁₋₁₂alkoxyC₁₋₁₂alkyl, C₁₋₁₂alkoxycarbonyl, aryloxy carbonyl, C₁₋₁₂alkylaminocarbonyl, arylaminocarbonyl, acyl, heterocyclyl, heteroaryl or heteroaralkyl groups[;], optionally substituted with one or more halogen, perhalomethyl, hydroxy, nitro or cyano;

R⁸ represents hydrogen, C₁₋₁₂alkyl, C₄₋₁₂-alkenynyl, C₂₋₁₂-alkenyl, C₂₋₁₂-alkynyl, aryl, aralkyl, heterocyclyl, heteroaryl or heteroaralkyl groups; optionally substituted with one or more halogen, perhalomethyl, hydroxy, nitro or cyano;

Y represents oxygen, sulphur or NR¹⁰, where R¹⁰ represents hydrogen, C₁₋₁₂alkyl, aryl, hydroxyC₁₋₁₂alkyl or aralkyl groups or when Y is NR¹⁰, R⁸ and R¹⁰ may form a 5 or 6 membered nitrogen containing ring, optionally substituted with one or more C₁₋₆alkyl;

n is an integer ranging from 1 to 4 and m is an integer ranging from 0 to 1;
or a pharmaceutically acceptable salt thereof.

2. (Amended) The compound according to claim 1, wherein ring A, fused to the ring containing X and N, represents a 5-6 membered cyclic ring optionally substituted with one or more hydrogen, halogen, perhalomethyl, hydroxy, cyano, or C₁₋₇alkyl, C₄₋₇-alkenynyl, C₂₋₇-alkenyl, C₂₋₇-alkynyl, C₁₋₇alkoxy, aryl, aryloxy, aralkyl, aralkoxy, heterocyclyl, heteroaryl, heteroaralkyl, heteroaryloxy, heteroaralkoxy, acyl, acyloxy, hydroxyC₁₋₇alkyl, amino, acylamino, C₁₋₇alkyl-amino, arylamino, aralkylamino, aminoC₁₋₇alkyl, C₁₋₇alkoxyC₁₋₇alkyl, aryloxyC₁₋₇alkyl, aralkoxyC₁₋₇alkyl, C₁₋₇alkylthio, thioC₁₋₇alkyl, C₁₋₇alkoxycarbonylamino, aryloxy carbonylamino, aralkoxycarbonylamino, -COR¹¹, or -SO₂R¹², wherein R¹¹ and R¹² independently of each other are selected from hydroxy, perhalomethyl or amino optionally substituted with one or more C₁₋₆alkyl, perhalomethyl or aryl; optionally substituted with one or more halogen, perhalomethyl, hydroxy or cyano.

7. (Amended) The compound according to claim 1, wherein ring B, fused to the ring containing X and N, represents a 5-6 membered cyclic ring optionally

substituted with one or more hydrogen, halogen, perhalomethyl, hydroxy, cyano, or C₁₋₇alkyl, C₄₋₇-alkenynyl, C₂₋₇-alkenyl, C₂₋₇-alkynyl, C₁₋₇alkoxy, aryl, aryloxy, aralkyl, aralkoxy, heterocyclyl, heteroaryl, heteroaralkyl, heteroaryloxy, heteroaralkoxy, acyl, acyloxy, hydroxyC₁₋₇alkyl, amino, acylamino, C₁₋₇alkyl-amino, arylamino, aralkylamino, aminoC₁₋₇alkyl, C₁₋₇alkoxyC₁₋₇alkyl, aryloxyC₁₋₇alkyl, aralkoxyC₁₋₇alkyl, C₁₋₇alkylthio, thioC₁₋₇alkyl, C₁₋₇alkoxycarbonyl-amino, aryloxy carbonylamino, aralkoxy carbonylamino, -COR¹¹, or -SO₂R¹², wherein R¹¹ and R¹² independently of each other are selected from hydroxy, perhalomethyl or amino optionally substituted with one or more C₁₋₆alkyl, perhalomethyl or aryl; optionally substituted with one or more halogen, perhalomethyl, hydroxy or cyano.

16. (Amended) The compound according to claim 1 wherein Q is -O- or -S-.

18. (Amended) The compound according to claim 1 wherein Ar represents arylene, heteroarylene, or a divalent heterocyclic group optionally substituted with one or more C₁₋₆alkyl or aryl;

R⁵ represents hydrogen, hydroxy, halogen, C₁₋₇alkoxy, C₁₋₇alkyl, C₄₋₇-alkenynyl, C₂₋₇-alkenyl, C₂₋₇-alkynyl; or R⁵ forms a bond together with R⁶,

R⁶ represents hydrogen, hydroxy, halogen, C₁₋₇alkoxy, C₁₋₇alkyl, C₄₋₇-alkenynyl, C₂₋₇-alkenyl, C₂₋₇-alkynyl; or R⁶ forms a bond together with R⁵,

R⁷ represents hydrogen, C₁₋₇alkyl, C₄₋₇-alkenynyl, C₂₋₇-alkenyl, C₂₋₇-alkynyl, aryl, aralkyl, C₁₋₇alkoxyC₁₋₇alkyl, C₁₋₇alkoxycarbonyl, aryloxy carbonyl, C₁₋₇alkylaminocarbonyl, arylaminocarbonyl, acyl, heterocyclyl, heteroaryl or heteroaralkyl groups;

R⁸ represents hydrogen, C₁₋₇alkyl, C₄₋₇-alkenynyl, C₂₋₇-alkenyl, C₂₋₇-alkynyl, aryl, aralkyl, heterocyclyl, heteroaryl or heteroaralkyl;

Y represents oxygen, sulphur or NR¹⁰, where R¹⁰ represents hydrogen, C₁₋₇alkyl, hydroxyC₁₋₇alkyl;

n is an integer ranging from 2 to 3 and m is an integer ranging from 0 to 1.

23. (Amended) The compound according to claim 1 wherein A is 5 membered cyclic ring containing S.

24. (Amended) The compound according to claim 1 wherein B is 5 membered cyclic ring containing S.
26. (Amended) The compound according to claim 1 wherein n is 2.
27. (Amended) The compound according to claim 1 wherein Q is -O-.
28. (Amended) The compound according to claim 1 wherein m is 1.
29. (Amended) The compound according to claim 1 wherein Ar is phenylene.
30. (Amended) The compound according to claim 1 wherein R⁶ is H.
31. (Amended) The compound according to claim 1 wherein R⁷ is ethyl.
32. (Amended) The compound according to claim 1 wherein Y is oxygen.
33. (Amended) The compound according to claim 1 wherein R⁸ is H.
34. (Amended) The compound according to claim 1 which is:
 3-{4-[2-(8,9-Dihydro-3,5-dithia-4-aza-cyclopenta[f]azulen-4-yl)-ethoxy]-phenyl}-2-ethoxy-propionic acid,
 3-{4-[2-(8,9-Dihydro-3,5-dithia-4-aza-cyclopenta[f]azulen-4-yl)-ethoxy]-phenyl}-2-methoxy-propionic acid,
 3-{4-[2-(8,9-Dihydro-3,5-dithia-4-aza-cyclopenta[f]azulen-4-yl)-ethoxy]-phenyl}-2-propoxy-propionic acid,
 3-{4-[2-(8,9-Dihydro-3,5-dithia-4-aza-cyclopenta[f]azulen-4-yl)-ethoxy]-phenyl}-2-benzyloxy-propionic acid,
 3-{4-[2-(8,9-Dihydro-3,5-dithia-4-aza-cyclopenta[f]azulen-4-yl)-ethyl]-phenyl}-2-ethoxy-propionic acid,

3-{4-[2-(8,9-Dihydro-3,5-dithia-4-aza-cyclopenta[f]azulen-4-yl)-ethyl]-phenyl}-2-methoxy-propionic acid,
 3-{4-[2-(8,9-Dihydro-3,5-dithia-4-aza-cyclopenta[f]azulen-4-yl)-ethyl]-phenyl}-2-propoxy-propionic acid,
 3-{4-[2-(8,9-Dihydro-3,5-dithia-4-aza-cyclopenta[f]azulen-4-yl)-ethyl]-phenyl}-2-benzyloxy-propionic acid,
 3-{4-[1-(8,9-Dihydro-3,5-dithia-4-aza-cyclopenta[f]azulen-4-yl)-methoxy]-phenyl}-2-ethoxy-propionic acid,
 3-{4-[1-(8,9-Dihydro-3,5-dithia-4-aza-cyclopenta[f]azulen-4-yl)-methoxy]-phenyl}-2-methoxy-propionic acid,
 3-{4-[1-(8,9-Dihydro-3,5-dithia-4-aza-cyclopenta[f]azulen-4-yl)-methoxy]-phenyl}-2-benzyloxy-propionic acid,
 3-{4-[3-(8,9-Dihydro-3,5-dithia-4-aza-cyclopenta[f]azulen-4-yl)-propoxy]-phenyl}-2-ethoxy-propionic acid,
 3-{4-[3-(8,9-Dihydro-3,5-dithia-4-aza-cyclopenta[f]azulen-4-yl)-propoxy]-phenyl}-2-methoxy-propionic acid,
 3-{4-[3-(8,9-Dihydro-3,5-dithia-4-aza-cyclopenta[f]azulen-4-yl)-propoxy]-phenyl}-2-benzyloxy-propionic acid,
 3-{4-[3-(8,9-Dihydro-3,5-dithia-4-aza-cyclopenta[f]azulen-4-yl)-propyl]-phenyl}-2-ethoxy-propionic acid,
 3-{4-[3-(8,9-Dihydro-3,5-dithia-4-aza-cyclopenta[f]azulen-4-yl)-propyl]-phenyl}-2-methoxy-propionic acid, or
 3-{4-[3-(8,9-Dihydro-3,5-dithia-4-aza-cyclopenta[f]azulen-4-yl)-propyl]-phenyl}-2-benzyloxy-propionic acid;
 or a pharmaceutically acceptable salt thereof.

36. (Amended) A pharmaceutical composition comprising as an active ingredient, the compound according to claim 1 or a pharmaceutically acceptable salt thereof together with a pharmaceutically acceptable carrier or diluent.

43. (Amended) A method for the treatment of conditions mediated by nuclear receptors, in particular the Peroxisome Proliferator-Activated Receptors (PPAR), the method

comprising administering to a subject in need thereof an effective amount of the compound according to claim 1 or a pharmaceutically acceptable salt thereof.

44. (Amended) A method for the treatment of diabetes, the method comprising administering to a subject in need thereof an effective amount of the compound according to claim 1 or a pharmaceutically acceptable salt thereof.

Please add the following new claims :

50. (New) The pharmaceutical composition of claim 36, wherein the compound is in a unit dosage form in the amount of between 0.05 to about 100 mg.

51. (New) The pharmaceutical composition of claim 37, wherein the compound is in a unit dosage form in the amount of between 0.1 to about 50 mg.

52. (New) The method of claim 44, wherein the compound is administered by oral, nasal, transdermal, pulmonary, or parenteral administration.

53. (New) A method for the treatment of obesity, the method comprising administering to a subject in need thereof an effective amount of the compound according to claim 1 or a pharmaceutically acceptable salt thereof.

54. (New) The method of claim 53, wherein the compound is administered by oral, nasal, transdermal, pulmonary, or parenteral administration.

REMARKS

Entry of this preliminary amendment is respectfully requested.

This application is a divisional of copending application no. 09/420,347. Claims 3-6, 8-15, 17, 19-22, 25, 35, 37-42 and 45-49 have been cancelled without prejudice or disclaimer. Claims 1, 2, 7, 16, 18, 23, 24, 26-34, 36, and 43-44 are amended to remove nonelected subject matter and to correct multiple dependencies. Claims 50-54 have been added. New claims 50-54 rewrite original claims 37, 41, and subject matter cancelled from pending claim 44. Claims 1, 2, 7, 16, 18, 23, 24, 26-34, 36, 43-44, and 50-54 are based on the corresponding claims as originally filed in the parent application and are directed to the subject matter of **Group IV** which has not elected in the parent application. No new matter is added.

Accordingly, claims 1, 2, 7, 16, 18, 23, 24, 26-34, 36, 43-44, and 50-54 are pending and at issue in this application.

It is believed that the claims are in condition for allowance, and a determination to that effect is earnestly solicited. The Examiner is hereby invited to contact the undersigned by telephone if there are any questions concerning this amendment or application.

Respectfully submitted,



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Date: November 27, 2001

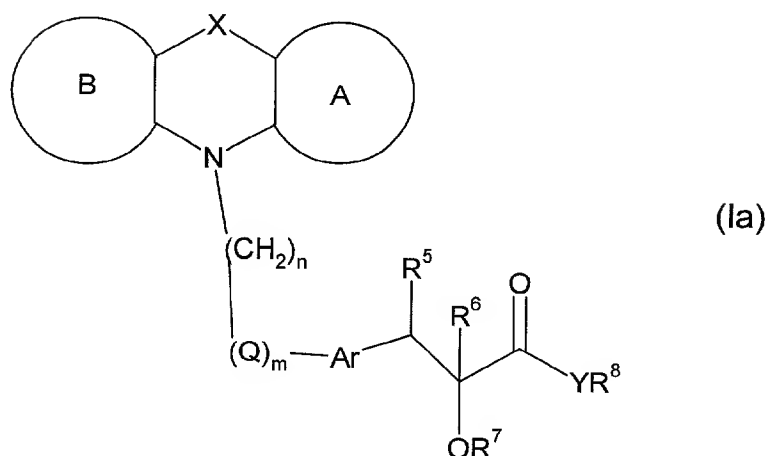


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PATENT TRADEMARK OFFICE

MARKED-UP VERSION OF THE CLAIMS SHOWING AMENDMENTS MADE

1. (Amended) A compound of formula (Ia)



wherein ring A_x fused to the ring containing X and N_x represents a 5-6 membered cyclic ring[,] optionally substituted with one or more halogen, perhalomethyl, hydroxy, nitro, cyano, formyl, or C₁₋₁₂alkyl, C₄₋₁₂-alkenynyl, C₂₋₁₂-alkenyl, C₂₋₁₂-alkynyl, C₁₋₁₂alkoxy, aryl, aryloxy, aralkyl, aralkoxy, heterocyclyl, heteroaryl, heteroaralkyl, heteroaryloxy, heteroaralkoxy, acyl, acyloxy, hydroxyC₁₋₁₂alkyl, amino, acylamino, C₁₋₁₂alkyl-amino, arylamino, aralkylamino, aminoC₁₋₁₂alkyl, C₁₋₁₂alkoxycarbonyl, aryloxycarbonyl, aralkoxycarbonyl, C₁₋₁₂alkoxyC₁₋₁₂alkyl, aryloxyC₁₋₁₂alkyl, aralkoxyC₁₋₁₂alkyl, C₁₋₁₂alkylthio, thioC₁₋₁₂alkyl, C₁₋₁₂alkoxycarbonylamino, aryloxycarbonylamino, aralkoxycarbonylamino, -COR¹¹, or -SO₂R¹², wherein R¹¹ and R¹² independently of each other are selected from hydroxy, halogen, perhalomethyl, C₁₋₆alkoxy or amino optionally substituted with one or more C₁₋₆alkyl, perhalomethyl or aryl; optionally substituted with one or more halogen, perhalomethyl, hydroxy, nitro or cyano;

ring B_x fused to the ring containing X and N_x represents a 5-6 membered cyclic ring[,] optionally substituted with one or more halogen, perhalomethyl, hydroxy, nitro, cyano, formyl, or C₁₋₁₂alkyl, C₄₋₁₂-alkenynyl, C₂₋₁₂-alkenyl, C₂₋₁₂-alkynyl,

C₁₋₁₂alkoxy, aryl, aryloxy, aralkyl, aralkoxy, heterocyclyl, heteroaryl, heteroaralkyl, heteroaryloxy, heteroaralkoxy, acyl, acyloxy, hydroxyC₁₋₁₂alkyl, amino, acylamino, C₁₋₁₂alkyl-amino, arylamino, aralkylamino, aminoC₁₋₁₂alkyl, C₁₋₁₂alkoxycarbonyl, aryloxycarbonyl, aralkoxycarbonyl, C₁₋₁₂alkoxyC₁₋₁₂alkyl, aryloxyC₁₋₁₂alkyl, aralkoxyC₁₋₁₂alkyl, C₁₋₁₂alkylthio, thioC₁₋₁₂alkyl, C₁₋₁₂alkoxycarbonylamino, aryloxycarbonylamino, aralkoxycarbonylamino, -COR¹¹, or -SO₂R¹², wherein R¹¹ and R¹² independently of each other are selected from hydroxy, halogen, perhalomethyl, C₁₋₆alkoxy or amino optionally substituted with one or more C₁₋₆alkyl, perhalomethyl or aryl; optionally substituted with one or more halogen, perhalomethyl, hydroxy, nitro or cyano;

X is [a valence bond, -(CHR⁹)-,] -(CHR⁹)-CH₂-, -CH=CH-, [-O-, -O-(CHR⁹)-, -S-(CHR⁹)-, -(NR⁹)-CH₂-,] -(CHR⁹)-CH=CH-, -(CHR⁹)-CH₂-CH₂-, [-(C=O)-, -O-CH₂-O-, -(NR⁹)-, -(NR⁹)-S(O₂)-,] -CH=(CR⁹)-, -(CO)-(CHR⁹)-, [-CH₂-(SO)-, -S-, -(SO)-, -(SO₂)-, -CH₂-(SO₂)-, -CH₂-O-CH₂-,] wherein R⁹ is hydrogen, halogen, hydroxy, nitro, cyano, formyl, C₁₋₁₂alkyl, C₁₋₁₂alkoxy, aryl, aryloxy, aralkyl, aralkoxy, heterocyclyl, heteroaryl, heteroaralkyl, heteroaryloxy, heteroaralkoxy, acyl, acyloxy, hydroxyalkyl, amino, acylamino, C₁₋₁₂alkyl-amino, arylamino, aralkylamino, aminoC₁₋₁₂alkyl, C₁₋₁₂alkoxycarbonyl, aryloxycarbonyl, aralkoxycarbonyl, C₁₋₁₂alkoxyC₁₋₁₂alkyl, aryloxyC₁₋₁₂alkyl, aralkoxyC₁₋₁₂alkyl, C₁₋₁₂alkylthio, thioC₁₋₁₂alkyl, C₁₋₁₂alkoxycarbonylamino, aryloxycarbonylamino, aralkoxycarbonylamino, -COR¹¹, or -SO₂R¹², wherein R¹¹ and R¹² independently of each other are selected from hydroxy, halogen, C₁₋₆alkoxy, amino optionally substituted with one or more C₁₋₆alkyl, perhalomethyl or aryl;

Q is -O-, -S-, >SO₂, >NR¹³, wherein R¹³ is hydrogen or C₁₋₆alkyl,

Ar represents arylene, heteroarylene, or a divalent heterocyclic group optionally substituted with one or more C₁₋₆alkyl or aryl;

R⁵ represents hydrogen, hydroxy, halogen, C₁₋₁₂alkoxy, C₁₋₁₂alkyl, C₄₋₁₂-alkenynyl,

C₂₋₁₂-alkenyl, C₂₋₁₂-alkynyl or aralkyl; optionally substituted with one or more halogen, perhalomethyl, hydroxy, nitro or cyano; or R⁵ forms a bond together with R⁶,

R⁶ represents hydrogen, hydroxy, halogen, C₁₋₁₂alkoxy, C₁₋₁₂alkyl, C₄₋₁₂-alkenynyl, C₂₋₁₂-alkenyl, C₂₋₁₂-alkynyl, acyl or aralkyl; optionally substituted with one or more halogen, perhalomethyl, hydroxy, nitro or cyano; or R⁶ forms a bond together with R⁵,

R⁷ represents hydrogen, C₁₋₁₂alkyl, C₄₋₁₂-alkenynyl, C₂₋₁₂-alkenyl, C₂₋₁₂-alkynyl, aryl, aralkyl, C₁₋₁₂alkoxyC₁₋₁₂alkyl, C₁₋₁₂alkoxycarbonyl, aryloxycarbonyl, C₁₋₁₂alkylaminocarbonyl, arylaminocarbonyl, acyl, heterocyclyl, heteroaryl or heteroaralkyl groups[;], optionally substituted with one or more halogen, perhalomethyl, hydroxy, nitro or cyano;

R⁸ represents hydrogen, C₁₋₁₂alkyl, C₄₋₁₂-alkenynyl, C₂₋₁₂-alkenyl, C₂₋₁₂-alkynyl, aryl, aralkyl, heterocyclyl, heteroaryl or heteroaralkyl groups; optionally substituted with one or more halogen, perhalomethyl, hydroxy, nitro or cyano;

Y represents oxygen, sulphur or NR¹⁰, where R¹⁰ represents hydrogen, C₁₋₁₂alkyl, aryl, hydroxyC₁₋₁₂alkyl or aralkyl groups or when Y is NR¹⁰, R⁸ and R¹⁰ may form a 5 or 6 membered nitrogen containing ring, optionally substituted with one or more C₁₋₆alkyl;

n is an integer ranging from 1 to 4 and m is an integer ranging from 0 to 1[, provided that A or B does not represent phenyl];
or a pharmaceutically acceptable salt thereof.

2. (Amended) [A] The compound according to claim 1, wherein ring A₁ fused to the ring containing X and N₁ represents a 5-6 membered cyclic ring[, optionally substituted with one or more hydrogen, halogen, perhalomethyl, hydroxy, cyano, or C₁₋₇alkyl, C₄₋₇-alkenynyl, C₂₋₇-alkenyl, C₂₋₇-alkynyl, C₁₋₇alkoxy, aryl, aryloxy, aralkyl, aralkoxy, heterocyclyl, heteroaryl, heteroaralkyl, heteroaryloxy, heteroaralkoxy, acyl, acyloxy, hydroxyC₁₋₇alkyl, amino, acylamino, C₁₋₇alkyl-amino, arylamino, aralkylamino, aminoC₁₋₇alkyl, C₁₋₇alkoxyC₁₋₇alkyl, aryloxyC₁₋₇alkyl, aralkoxyC₁₋₇alkyl, C₁₋₇alkylthio, thioC₁₋₇alkyl, C₁₋₇alkoxycarbonylamino,

aryloxycarbonylamino, aralkoxycarbonylamino, -COR¹¹, or -SO₂R¹², wherein R¹¹ and R¹² independently of each other are selected from hydroxy, perhalomethyl or amino optionally substituted with one or more C₁₋₆alkyl, perhalomethyl or aryl; optionally substituted with one or more halogen, perhalomethyl, hydroxy or cyano.

7. (Amended) [A] The compound according to [anyone of the preceding claims] claim 1, wherein ring B₂ fused to the ring containing X and N₂ represents a 5-6 membered cyclic ring[,] optionally substituted with one or more hydrogen, halogen, perhalomethyl, hydroxy, cyano, or C₁₋₇alkyl, C₄₋₇-alkenynyl, C₂₋₇-alkenyl, C₂₋₇-alkynyl, C₁₋₇alkoxy, aryl, aryloxy, aralkyl, aralkoxy, heterocyclyl, heteroaryl, heteroaralkyl, heteroaryloxy, heteroaralkoxy, acyl, acyloxy, hydroxyC₁₋₇alkyl, amino, acylamino, C₁₋₇alkyl-amino, arylamino, aralkylamino, aminoC₁₋₇alkyl, C₁₋₇alkoxyC₁₋₇alkyl, aryloxyC₁₋₇alkyl, aralkoxyC₁₋₇alkyl, C₁₋₇alkylthio, thioC₁₋₇alkyl, C₁₋₇alkoxycarbonylamino, aryloxycarbonylamino, aralkoxycarbonylamino, -COR¹¹, or -SO₂R¹², wherein R¹¹ and R¹² independently of each other are selected from hydroxy, perhalomethyl or amino optionally substituted with one or more C₁₋₆alkyl, perhalomethyl or aryl; optionally substituted with one or more halogen, perhalomethyl, hydroxy or cyano.

16. (Amended) [A] The compound according to [anyone of the preceding claims] claim 1 wherein Q is -O- or -S-.

18. (Amended) [A] The compound according to [anyone of the preceding claims] claim 1 wherein Ar represents arylene, heteroarylene, or a divalent heterocyclic group optionally substituted with one or more C₁₋₆alkyl or aryl; R⁵ represents hydrogen, hydroxy, halogen, C₁₋₇alkoxy, C₁₋₇alkyl, C₄₋₇-alkenynyl, C₂₋₇-alkenyl, C₂₋₇-alkynyl; or R⁵ forms a bond together with R⁶, R⁶ represents hydrogen, hydroxy, halogen, C₁₋₇alkoxy, C₁₋₇alkyl, C₄₋₇-alkenynyl, C₂₋₇-alkenyl, C₂₋₇-alkynyl; or R⁶ forms a bond together with R⁵, R⁷ represents hydrogen, C₁₋₇alkyl, C₄₋₇-alkenynyl, C₂₋₇-alkenyl, C₂₋₇-alkynyl, aryl, aralkyl, C₁₋₇alkoxyC₁₋₇alkyl, C₁₋₇alkoxycarbonyl, aryloxycarbonyl, C₁₋₇alkylaminocarbonyl, arylaminocarbonyl, acyl, heterocyclyl, heteroaryl or heteroaralkyl groups;

R⁸ represents hydrogen, C₁₋₇alkyl, C₄₋₇-alkenynyl, C₂₋₇-alkenyl, C₂₋₇-alkynyl, aryl, aralkyl, heterocyclyl, heteroaryl or heteroaralkyl;

Y represents oxygen, sulphur or NR¹⁰, where R¹⁰ represents hydrogen, C₁₋₇alkyl, hydroxyC₁₋₇alkyl;

n is an integer ranging from 2 to 3 and m is an integer ranging from 0 to 1.

23. (Amended) [A] The compound according to [anyone of the preceding claims] claim 1 wherein A is 5 membered cyclic ring containing S.

24. (Amended) [A] The compound according to [anyone of the preceding claims] claim 1 wherein B is 5 membered cyclic ring containing S.

26. (Amended) [A] The compound according to [anyone of the preceding claims] claim 1 wherein n is 2.

27. (Amended) [A] The compound according to [anyone of the preceding claims] claim 1 wherein Q is -O-.

28. (Amended) [A] The compound according to [anyone of the preceding claims] claim 1 wherein m is 1.

29. (Amended) [A] The compound according to [anyone of the preceding claims] claim 1 wherein Ar is phenylene.

[In another preferred embodiment, the present invention is concerned with compounds of formula I wherein R⁵ is H.]

30. (Amended) [A] The compound according to [anyone of the preceding claims] claim 1 wherein R⁶ is H.

31. (Amended) [A] The compound according to [anyone of the preceding claims] claim 1 wherein R⁷ is ethyl.

32. (Amended) [A] The compound according to [anyone of the preceding claims] claim 1 wherein Y is oxygen.

33. (Amended) [A] The compound according to [anyone of the preceding claims] claim 1 wherein R⁸ is H.

34. (Amended) The compound according to claim 1 which is:

3-{4-[2-(8,9-Dihydro-3,5-dithia-4-aza-cyclopenta[f]azulen-4-yl)-ethoxy]-phenyl}-2-ethoxy-propionic acid,

3-{4-[2-(8,9-Dihydro-3,5-dithia-4-aza-cyclopenta[f]azulen-4-yl)-ethoxy]-phenyl}-2-methoxy-propionic acid,

3-{4-[2-(8,9-Dihydro-3,5-dithia-4-aza-cyclopenta[f]azulen-4-yl)-ethoxy]-phenyl}-2-propoxy-propionic acid,

3-{4-[2-(8,9-Dihydro-3,5-dithia-4-aza-cyclopenta[f]azulen-4-yl)-ethoxy]-phenyl}-2-benzyloxy-propionic acid,

3-{4-[2-(8,9-Dihydro-3,5-dithia-4-aza-cyclopenta[f]azulen-4-yl)-ethyl]-phenyl}-2-ethoxy-propionic acid,

3-{4-[2-(8,9-Dihydro-3,5-dithia-4-aza-cyclopenta[f]azulen-4-yl)-ethyl]-phenyl}-2-methoxy-propionic acid,

3-{4-[2-(8,9-Dihydro-3,5-dithia-4-aza-cyclopenta[f]azulen-4-yl)-ethyl]-phenyl}-2-propoxy-propionic acid,

3-{4-[2-(8,9-Dihydro-3,5-dithia-4-aza-cyclopenta[f]azulen-4-yl)-ethyl]-phenyl}-2-benzyloxy-propionic acid,

3-{4-[1-(8,9-Dihydro-3,5-dithia-4-aza-cyclopenta[f]azulen-4-yl)-methoxy]-phenyl}-2-ethoxy-propionic acid,

3-{4-[1-(8,9-Dihydro-3,5-dithia-4-aza-cyclopenta[f]azulen-4-yl)-methoxy]-phenyl}-2-methoxy-propionic acid,

3-{4-[1-(8,9-Dihydro-3,5-dithia-4-aza-cyclopenta[f]azulen-4-yl)-methoxy]-phenyl}-2-benzyloxy-propionic acid,

3-{4-[3-(8,9-Dihydro-3,5-dithia-4-aza-cyclopenta[f]azulen-4-yl)-propoxy]-phenyl}-2-ethoxy-propionic acid,

2-methoxy-3-(4-(3-(4,5,9-triaza-fluoren-9-yl)-propoxy)-phenyl)-propionic acid,
 2-benzyloxy-3-(4-(3-(4,5,9-triaza-fluoren-9-yl)-propoxy)-phenyl)-propionic acid,
 2-propoxy-3-(4-(3-(4,5,9-triaza-fluoren-9-yl)-propoxy)-phenyl)-propionic acid,
 2-ethoxy-3-(4-(3-(4,5,9-triaza-fluoren-9-yl)-propyl)-phenyl)-propionic acid,
 2-methoxy-3-(4-(3-(4,5,9-triaza-fluoren-9-yl)-propyl)-phenyl)-propionic acid,
 2-benzyloxy-3-(4-(3-(4,5,9-triaza-fluoren-9-yl)-propyl)-phenyl)-propionic acid,
 2-propoxy-3-(4-(3-(4,5,9-triaza-fluoren-9-yl)-propyl)-phenyl)-propionic acid,
 2-ethoxy-3-(4-(2-(1,8,9-triaza-fluoren-9-yl)-ethoxy)-phenyl)-propionic acid,
 2-methoxy-3-(4-(2-(1,8,9-triaza-fluoren-9-yl)-ethoxy)-phenyl)-propionic acid,
 2-propoxy-3-(4-(2-(1,8,9-triaza-fluoren-9-yl)-ethoxy)-phenyl)-propionic acid,
 2-benzyloxy-3-(4-(2-(1,8,9-triaza-fluoren-9-yl)-ethoxy)-phenyl)-propionic acid,
 2-methoxy-3-(4-(1-(1,8,9-triaza-fluoren-9-yl)-methoxy)-phenyl)-propionic acid,
 2-ethoxy-3-(4-(1-(1,8,9-triaza-fluoren-9-yl)-methoxy)-phenyl)-propionic acid,
 2-propoxy-3-(4-(1-(1,8,9-triaza-fluoren-9-yl)-methoxy)-phenyl)-propionic acid,
 2-benzyloxy-3-(4-(1-(1,8,9-triaza-fluoren-9-yl)-methoxy)-phenyl)-propionic acid,
 2-ethoxy-3-(4-(3-(1,8,9-triaza-fluoren-9-yl)-propoxy)-phenyl)-propionic acid,
 2-methoxy-3-(4-(3-(1,8,9-triaza-fluoren-9-yl)-propoxy)-phenyl)-propionic acid,
 2-propoxy-3-(4-(3-(1,8,9-triaza-fluoren-9-yl)-propoxy)-phenyl)-propionic acid,
 2-benzyloxy-3-(4-(3-(1,8,9-triaza-fluoren-9-yl)-propoxy)-phenyl)-propionic acid,
 2-ethoxy-3-(4-(3-(1,8,9-triaza-fluoren-9-yl)-propyl)-phenyl)-propionic acid,
 2-methoxy-3-(4-(3-(1,8,9-triaza-fluoren-9-yl)-propyl)-phenyl)-propionic acid,
 2-propoxy-3-(4-(3-(1,8,9-triaza-fluoren-9-yl)-propyl)-phenyl)-propionic acid,
 2-benzyloxy-3-(4-(3-(1,8,9-triaza-fluoren-9-yl)-propyl)-phenyl)-propionic acid,
 3-(4-(2-(dithieno[2,3-*b*;3',2'-*d*]pyrrol-7-yl)-ethoxy)-phenyl)-2-ethoxy-propionic acid,
 3-(4-(2-(dithieno[2,3-*b*;3',2'-*d*]pyrrol-7-yl)-ethoxy)-phenyl)-2-methoxy-propionic acid,
 3-(4-(2-(dithieno[2,3-*b*;3',2'-*d*]pyrrol-7-yl)-ethoxy)-phenyl)-2-propoxy-propionic acid,
 3-(4-(2-(dithieno[2,3-*b*;3',2'-*d*]pyrrol-7-yl)-ethoxy)-phenyl)-2-benzyloxy-propionic acid,
 3-(4-(1-(dithieno[2,3-*b*;3',2'-*d*]pyrrol-7-yl)-methoxy)-phenyl)-2-methoxy-propionic acid,
 3-(4-(1-(dithieno[2,3-*b*;3',2'-*d*]pyrrol-7-yl)-methoxy)-phenyl)-2-ethoxy-propionic acid,
 3-(4-(1-(dithieno[2,3-*b*;3',2'-*d*]pyrrol-7-yl)-methoxy)-phenyl)-2-propoxy-propionic acid,
 3-(4-(1-(dithieno[2,3-*b*;3',2'-*d*]pyrrol-7-yl)-methoxy)-phenyl)-2-benzyloxy-propionic acid,
 3-(4-(3-(dithieno[2,3-*b*;3',2'-*d*]pyrrol-7-yl)-propoxy)-phenyl)-2-ethoxy-propionic acid,

3-(4-(3-(4*H*-1,7-dithia-8-aza-*s*-indacen-8-yl)-propoxy)-phenyl)-2-methoxy-propionic acid,
 3-(4-(3-(4*H*-1,7-dithia-8-aza-*s*-indacen-8-yl)-propoxy)-phenyl)-2-propoxy-propionic acid,
 3-(4-(3-(4*H*-1,7-dithia-8-aza-*s*-indacen-8-yl)-propoxy)-phenyl)-2-benzyloxy-propionic acid,
 3-(4-(3-(4*H*-1,7-dithia-8-aza-*s*-indacen-8-yl)-propyl)-phenyl)-2-ethoxy-propionic acid,
 3-(4-(3-(4*H*-1,7-dithia-8-aza-*s*-indacen-8-yl)-propyl)-phenyl)-2-methoxy-propionic acid,
 3-(4-(3-(4*H*-1,7-dithia-8-aza-*s*-indacen-8-yl)-propyl)-phenyl)-2-propoxy-propionic acid,
 3-(4-(3-(4*H*-1,7-dithia-8-aza-*s*-indacen-8-yl)-propyl)-phenyl)-2-benzyloxy-propionic acid,
 2-ethoxy-3-(4-(2-(4-oxa-1,7-dithia-8-aza-*s*-indacen-8-yl)-ethoxy)-phenyl)-propionic acid,
 2-methoxy-3-(4-(2-(4-oxa-1,7-dithia-8-aza-*s*-indacen-8-yl)-ethoxy)-phenyl)-propionic acid,
 2-propoxy-3-(4-(2-(4-oxa-1,7-dithia-8-aza-*s*-indacen-8-yl)-ethoxy)-phenyl)-propionic acid,
 2-propoxy-3-(4-(2-(4-oxa-1,7-dithia-8-aza-*s*-indacen-8-yl)-ethoxy)-phenyl)-propionic acid,
 2-benzyloxy-3-(4-(2-(4-oxa-1,7-dithia-8-aza-*s*-indacen-8-yl)-ethoxy)-phenyl)-propionic acid,
 2-ethoxy-3-(4-(1-(4-oxa-1,7-dithia-8-aza-*s*-indacen-8-yl)-methoxy)-phenyl)-propionic acid,
 2-methoxy-3-(4-(1-(4-oxa-1,7-dithia-8-aza-*s*-indacen-8-yl)-methoxy)-phenyl)-propionic acid,
 2-propoxy-3-(4-(1-(4-oxa-1,7-dithia-8-aza-*s*-indacen-8-yl)-methoxy)-phenyl)-propionic acid,
 2-benzyloxy-3-(4-(1-(4-oxa-1,7-dithia-8-aza-*s*-indacen-8-yl)-methoxy)-phenyl)-propionic
 acid,
 2-ethoxy-3-(4-(3-(4-oxa-1,7-dithia-8-aza-*s*-indacen-8-yl)-propoxy)-phenyl)-propionic acid,
 2-methoxy-3-(4-(3-(4-oxa-1,7-dithia-8-aza-*s*-indacen-8-yl)-propoxy)-phenyl)-propionic acid,
 2-propoxy-3-(4-(3-(4-oxa-1,7-dithia-8-aza-*s*-indacen-8-yl)-propoxy)-phenyl)-propionic acid,
 2-benzyloxy-3-(4-(3-(4-oxa-1,7-dithia-8-aza-*s*-indacen-8-yl)-propoxy)-phenyl)-propionic
 acid,
 2-ethoxy-3-(4-(3-(4-oxa-1,7-dithia-8-aza-*s*-indacen-8-yl)-propyl)-phenyl)-propionic acid,
 2-methoxy-3-(4-(3-(4-oxa-1,7-dithia-8-aza-*s*-indacen-8-yl)-propyl)-phenyl)-propionic acid,
 2-propoxy-3-(4-(3-(4-oxa-1,7-dithia-8-aza-*s*-indacen-8-yl)-propyl)-phenyl)-propionic acid,
 2-benzyloxy-3-(4-(3-(4-oxa-1,7-dithia-8-aza-*s*-indacen-8-yl)-propyl)-phenyl)-propionic
 acid];

or a pharmaceutically acceptable salt thereof.

36. (Amended) A pharmaceutical composition comprising[,] as an active ingredient, [a] the compound according to [any one of the preceding compound claims] claim 1 or a

pharmaceutically acceptable salt thereof together with a pharmaceutically acceptable carrier or diluent.

43. (Amended) A method for the treatment [and/or prevention] of conditions mediated by nuclear receptors, in particular the Peroxisome Proliferator-Activated Receptors (PPAR), the method comprising administering to a subject in need thereof an effective amount of [a] the compound according to [any one of the preceding compound claims] claim 1 or a pharmaceutically acceptable salt thereof[, or of a composition according to anyone of the preceding claims 36-41].

44. (Amended) A method for the treatment [and/or prevention] of diabetes [and/or obesity], the method comprising administering to a subject in need thereof an effective amount of [a] the compound according to [anyone of the preceding compound claims] claim 1 or a pharmaceutically acceptable salt thereof[, or of a composition according to anyone of the preceding claims 36-41].